REMARKS

Status of the Claims

Claims 1, 3-6, 8, and 9-24 are pending. Claims 1, 6, and 21 are amended. Claims 2 and 7 are canceled.

Interview Summary

As indicated in the Record, the Examiner graciously permitted a personal interview with Applicant's representative on February 21, 2008. The contents of the interview are accurately summarized on the Examiner Interview Summary form that has been entered. Additional specifics of the interview are discussed in connection with the outstanding rejections, below.

Issues Under 35 U.S.C. § 112

Claims 1-8, 17, 18, and 21 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement.

This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

This rejection was discussed in detail at the interview. While Applicants respectfully maintain their position regarding the overlap in scope, it was agreed that the claims, as amended

more closely resemble the language of the specification. See, for example, page 3, lines 14-16.

Accordingly, Applicant's respectfully submit that this rejection should be withdrawn.

Issues Under 35 U.S.C. § 103

Claims 1-8 and 17-21 are rejected under 35 U.S.C. § 103 as allegedly being obvious over Lopez-Berenstein et al. (US '167) in view of US Patent No. 4,902,789 to Michel et al. (US '789), or US Patent No. 4,308,375 to Tsang (US '375). This rejection is respectfully traversed.

These references are discussed extensively in the record.

In summary, the primary reference, Lopez-Berenstein, fails to even address amphotericin B purity at all in the same terms as the present invention. Lopez-Berenstein is concerned with encapsulation. At col. 4, lines 8-19, achieving 100% encapsulation is discussed. As discussed in the Office Action, this reference does "not disclose purification of amphotericin B." See page 4 of the Office Action.

The Office Action further indicates that since purification was well known at the time (as per the Michel et al. or Tang secondary references), one would be motivated to purify the amphotericin B composition of Lopez-Berenstein.

Applicants respectfully submit that there is no indication that one of ordinary skill in the art would view the combination of references in such a light.

As indicated previously, the method of Michel et al. relates to residue on ignition, an inappropriate identifier of polyenes. See the previous response at pages 10-11, and the Kramer Declaration at paragraphs 4-5. The Tang reference discloses a method of purifying amphotericin B with an ion exchange column that removes gram positive and gram negative bacteria, which does not address the polyene impurity issues that are addressed by the present invention.

Thus, as previously indicated, the notion that "since purification of amphotericin B was well known in the art at the time the claimed invention was made as disclosed by [the secondary references]..." is not a correct interpretation of the secondary references. Applicants respectfully submit that there is no basis in the prior art references that the claimed compositions would be obvious, particularly since it is clear that the "purification" methods relied on are not appropriate to arrive at the instant claims. There is no objective, reasoned statement in the Office Action to suggest otherwise. It is the Applicants that discovered the need for the claimed purification products and a method for achieving them.

Furthermore, there is an inconsistency in the Office Action in connection with the Declaration of Dr. Kramer. This inconsistency was also discussed during the interview. The Office Action relies on the Declaration as stating "that the product of recrystallization method 1 disclosed *by the art of record* result [sic] in an apparent product having 95% [purity]." See the Office Action at page 4 (emphasis added).

Applicants respectfully submit that this is not a correct interpretation of the Declaration.

Paragraphs 10-15 of the Kramer Declaration address the request in the previous Office Action for a showing of "unexpected results relating to *obtaining* the subject compound having the claimed purity levels." (Emphasis added.) The Declaration should not be interpreted as having prepared compositions as per the prior art, or some type of combination of bits and pieces of the prior art.

The Kramer Declaration showed that HPLC was an effective method of *obtaining* the subject claimed active ingredient. As discussed during the interview, the Declaration shows that the HPLC is a superior and unexpected purification method compared to the liquid:liquid extraction and recrystallization method in part because of its improved consistency and improved results. See paragraph 13 in the Kramer Declaration. The Office Action appears to link the comparison purification method with the cited prior art. Such is not a proper link.

Thus, the Office Action fails to present a *prima facie* case of obviousness because there is no established relationship between the cited prior art and claimed invention.

Finally, the Office Action states that "a person would have expected less side effects with administration of purified amphotericin B." See page 4. Applicants respectfully submit that with respect to the compositions as claimed, there is no objective, technical support for this position, and with respect to the present invention the expectations set forth by the Examiner is not the case.

As indicated in the Specification, amphotericin B is used to treat a variety of fungal

infections despite the high incidence of side effects. The present inventors have discovered a source for many of the side effects. For example, it was discovered by the present inventors that non-Amphotericin B polyenes are a significant side effect source. This was not previously known, and is surprising when compared to the many prior attempts to formulate a safer amphotericin B product. Encapsulation is one example of an attempt to formulate a safer amphotericin product.

Additionally, the attached Declaration of Dr. John D. Cleary shows examples of the superior and unexpected results of the present invention. In summary, the compositions of the present invention, when compared to commercial, USP preparations, demonstrated an ability to apply a 10-fold higher dose and obtain only about half the renal toxicity. Additionally, the Declaration shows that the mortality rate in infected mice treated with the claimed invention was about half the mortality rate of mice treated with commercial, USP preparations. Additionally, this trend occurs despite the 10-fold greater dose of the composition of the present invention. As indicated in the Declaration, this result is superior and unexpected.

In summary, it is clear that the instant rejection fails to present a *prima facie* case of obviousness, especially in view of the fact that the secondary references fail to remedy or even suggest the deficiencies of the primary reference. Therefore, Applicants respectfully submit that the obviousness rejection should be withdrawn. Assuming, *arguendo*, that any *prima facie* case existed, it would be rebutted by the Cleary Declaration.

In view of the above, Applicants request that this rejection be withdrawn.

Additionally, Applicants respectfully submit that each issue precluding allowance has been adequately addressed.

Petition for Extension of Time

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for a three-month extension of time for filing a response to the outstanding Office Action. Payment for the extension of time fee is being submitted with the electronic filing of this response.

The Office is authorized to charge any deficiency or credit any overpayment associated with the filing of this application to Deposit Account 50-2752.

Finally, please contact the undersigned if there are any questions regarding this Amendment or the application in general.

Respectfully submitted,

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